REMARKS

Upon entry of the amendment, claims 1-11 and 18-23 are canceled, claims 12 and 14-17 are amended, and new claims 24-35 are added.

Upon entry of the amendment, claims 12-17 and 24-35 are pending.

Support for Amendments / No New Issues Raised After Final Rejection

Support for the amendments can be found throughout the specification as originally filed. For example, support for claim 12 can be found in the specification at pages 8 (lines 1-8) and page 13 (line 14) through page 14 (line 8). Amended claim 14 corresponds to previous claim 15. Support for amended claim 15 can be found at page 13, 3rd and 4th full paragraphs. Support for new claims 24-29 can be found in previous claims 13-17 and in the specification at page 12, last paragraph, page 13, 3rd and 4th full paragraphs, and in Examples 1 and 2. New claims 30-35 correspond to canceled claims 18-23 with the addition of "soft tissue sarcoma" to claim 30, with support for the phrase found in the specification at page 16 (lines 1-10). New claims 30-35 include additional dependencies, with support found in the specification as originally filed.

No new issues for consideration are raised by entry of the amendments. The examination of the previous claims has already included a discussion of the dosing range levels of Et 743 (see Office Action, page 3, lines 4-7 and page 4, lines 1-4) as well as cancer types (see Office Action, page 2, lines 10 and 16). Therefore, the present amendments raise no new issues for consideration.

Information Disclosure Statement / Related Case Statement

Applicants hereby submit an Information Disclosure Statement / Related Case Statement.

Copies of WO 99/58125, WO 99/51238, and Valoti (Clin. Cancer Res., vol. 4, pages 1977-83, Aug 1998) are not provided because the references are already of record and entered in the electronic file for this application (see PAIR entries for November 13, 2001 under the headings "Foreign Reference" or "NPL Documents" respectively).

Drawing

Applicants respectfully request an indication of acceptability of the drawing submitted on November 13, 2001 (see PAIR entry under heading "Drawings").

Rejection Under Provisional Obviousness Double-Patenting

The rejection of claims 12-22 under provisional obviousness double-patenting as unpatentable over claims 1-29 of co-pending US 10/492,320 is maintained by the Examiner. Because the rejection is provisional and US 10/492,320 is awaiting a first office action on the merits following a restriction requirement, Applicants respectfully request that the rejection be held in abeyance pending the determination of patentable subject matter. Applicants suggest that if all other rejections are overcome, it is appropriate to withdraw the provisional double-patenting rejection and allow the instant application to issue, and apply any double-patenting rejections deemed necessary by the Examiner to the co-pending application, as directed by the MPEP:

> If the "provisional" double patenting rejection is the only rejection remaining in that application, the examiner should then withdraw that rejection and permit the application to issue as a patent, thereby converting the "provisional" double patenting rejection in

the other application(s) into a double patenting rejection at the time the one application issues as a patent. (MPEP 804.1B)

Rejection Under 35 U.S.C. § 103(a)

Claims 12-23 are rejected under 35 U.S.C. § 103(a) for being unpatentable over Taamma et al. (Eur. J. Cancer) in view of Barrera et al. (Proceedings of the American Association of Cancer Research). See Office Action, June 9, 2006, pages 2-4. Applicants respectfully traverse to the extent that the rejection may be applied to the claims upon entry of the above amendment.

U.S. case law holds that a proper obviousness inquiry requires consideration of three factors: (1) the prior art reference or references must teach or suggest all the claim limitatons; (2) the prior art must teach, motivate, or suggest to those of ordinary skill in the art that they should make the claimed invention or practice the claimed method; and (3) the prior art must establish that in making the claimed invention or practicing the claimed method, there would have been a reasonable expectation of success. *See, e.g., In re Vaeck*, 947 F.2d, 488, 493 (Fed. Cir. 1991); *See also* MPEP 2142.

1) Failure of the references to teach all of the claimed elements

Claim 12 includes the element of "administering at a dose level of about 500 to a1650 microgram/m^2 of Et 743". Claims 15 and 26 include the subranges about 1000 to about 1650 micrograms/m^2 and about 1000 to about 1500 micrograms/m^2, respectively. Claim 27 requires a dose level of about 1500 micrograms/m^2. The Office Action states that "Taamma teaches administration of Et-743 to human patients in Phase I clinical trials" (OA, page 3). However, Taamma is limited to phase I clinical study of Et-743 at doses of 50, 100, 200 and 400

micrograms/m^2. Additionally, Barrera does not cure the deficiencies of Taamma. Although Barrera discloses that Et-743 is entering Phase II clinical trials, Barrera fails to provide any dosing of Et 743. Accordingly, Applicants respectfully submit that neither Taamma nor Barrera, alone or in combination, teach or suggest administering at a dose level of about 500 to 1650 micrograms/m^2 of Et 743, about 1000 to 1650 micrograms/m^2 of Et 743, about 1000 to 1500 micrograms/m^2 of Et 743, and about 1500 micrograms/m^2 of Et 743, respectively. For at least the reason that the references cited by the Examiner fail to teach or suggest all the claim limitatons, Applicants request that the rejection be withdrawn.

2) Failure of the references to provide motivation

Applicants respectfully submit that combined references, in failing to teach the claimed ranges, thereby also fail to provide motivation for the claimed ranges. The Examiner indicates that one "would have been motivated to seek an optimal dosing regimen with respect to infusion times and intervals of administration through no more than routine experimentation" (Office Action, page 4, 2nd full paragraph). Applicants respectfully disagree with the Examiner's characterization of the many variables involved in human clinical trials of potentially toxic compounds to arrive at a pharmacotherapeutic window as "routine experimentation". Even assuming, *arguendo*, that routine experimentation is involved in clinical trials, the courts have commented on "routine testing" as follows:

> Due to the fact that chemistry is still largely an empirical science it is easy to characterize inventions in the chemical field as but the result of "routine testing." It cannot be denied that "routine testing" is an essential part of many inventions in the chemical field. But even "routine" testing, whatever that may be, must be guided and directed by the mental concept of the inventor.

In re Fay et al., 347 F2d 597 CCPA 1965). The courts comments with respect to chemistry are even more applicable to biological systems such as human clinical trials. The references cited by

the Examiner provide no direction or motivation for choosing which variables of all the multitude of variables should be evaluated, and what ranges should be applied for those variables.

3) Failure of the references to provide reasonable expectation of success

The present invention is directed to a method of treatment of a human patient for cancer comprising administering Et 743 at a dose level of about 500 to about 1650 micrograms/m^2 body surface area in cycles by intravenous infusion at intervals of about 1-6 weeks with an infusion time of about 2 to about 24 hours wherein said treatment results in a reduction in tumor size. Even if, *arguendo*, the claimed elements could have been arrived at by testing all possibilities through the Examiner's suggested "routine optimization", there is no reasonable expectation of success in arriving at the above cancer treatment through routine optimization.

Fields such as petroleum refining and catalytic production of chemicals are amenable to routine optimization through varying reaction temperatures, for example. Logically, when one has a chemical process that is shown to work, one can vary the parameters and at some point arrive at a maximum output.

In treating diseases such as cancer, however, the same cannot be said. It is well-known in the pharmaceutical field that drug candidates often fail during clinical trials. Drug candidates can fail for any number of reasons, such as lack of efficacy *in vivo* despite activity *in vitro* or an unacceptably narrow window of therapeutic efficacy when compared to toxicity effects. In other words, lots of drug trials for cancer fail to arrive at the particular dosing regimen resulting in reduction of tumor size despite the fact that the drugs have entered clinical trials.

Routine experimentation is likely to result in a failed drug candidate. If finding an efficacious drug were merely routine based on phase I trials, then many more cancer drugs would be available. In cancer, the end-point of a reduction in tumor size while maintaining acceptable toxicity levels is not guaranteed. Simply put, there is no reasonable expectation that one of ordinary skill in the art will achieve a reduction in tumor size according to the claims based on entry of the drug candidate in Phase I clinical trials. The best that can be said of the cited references is that the end result of tumor size reduction is a desired but in no way certain outcome of their teachings.

CONCLUSION

Based on the foregoing amendments and remarks, Applicants respectfully request reconsideration and withdrawal of the rejection of claims and allowance of this application.

AUTHORIZATION

The Commissioner is hereby authorized to charge any additional fees which may be required for consideration of this Amendment to Deposit Account No. **50-3732**, Order No. 13566.105002.

In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. **50-3732**, Order No. 13566.105002.

Respectfully submitted,
King & Spalding, LLP

Dated: December 7, 2006 By: _____

Kenneth H. Sonnenfeld / Michael A. Willis
Reg. No. 33,285 / Reg. No. 53,913

Customer Number 65989
Correspondence Address:

King & Spalding
1185 Avenue of the Americas
New York, NY 10036-4003
(212) 556-2100 Telephone
(212) 556-2222 Facsimile